PATENT
Attorney Docket Nos. 084/US/PCT2/US and 00537-188002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:	EXAMINER: **Coleman, Brenda Libby**
GORDON, Thomas D. *et al.*	ART UNIT: **1624**
APPLICATION NO.: **09/868,356**	
FILED: **August 10, 2001**	
FOR: **PRENYL TRANSFERASE INHIBITORS**	

I hereby certify under 37 CFR 1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Assistant Commissioner of Patents, Washington, D.C. 20231.
Date of Deposit: January 14, 2004
Dawn Janelle
Dawn M. Janelle

Mail Stop Non-Fee Amendment
Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

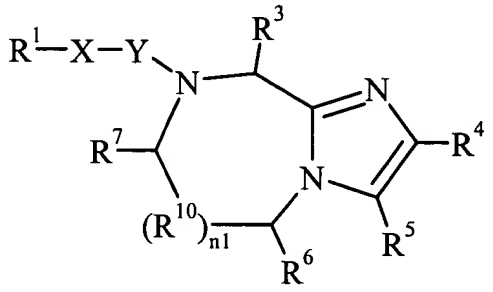
REPLY UNDER 37 C.F.R. §1.111

In response to the Office Action (Paper No. 11) mailed on July 14, 2003, the period for response there having been extended so as to expire on January 14, 2004 pursuant to Applicants' Petition for Extension of Time filed concurrently with this Reply, please amend the above-identified application as follows.

The present amendments follow the revised format procedure mandated in 68 Fed. Reg. 38611 published June 30, 2003.

COMPLETE LISTING OF ALL CLAIMS, WITH MARKINGS AND STATUS IDENTIFIERS
(Currently amended claims showing deletions ~~by strikethrough~~ and additions by underlining)

1 (currently amended): A compound of formula I,



(I)

wherein

n1 is 0 ~~or 1~~;

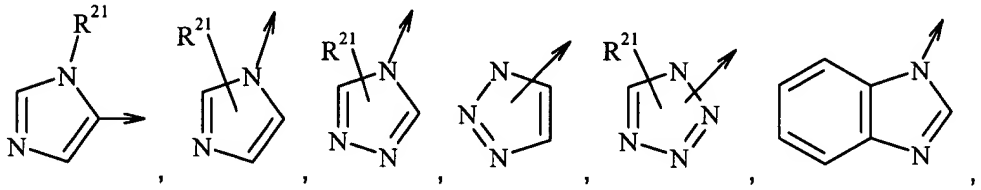
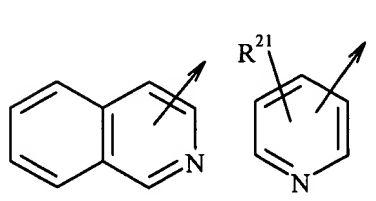
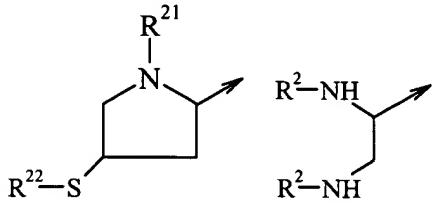
X is, independently for each occurrence, $(CHR^{11})_{n3}(CH_2)_{n4}Z(CH_2)_{n5}$;

Z is O, $N(R^{12})$, S, or a bond;

n3 is, independently for each occurrence, 0 or 1;

n4 and n5 each is, independently for each occurrence, 0, 1, 2, or 3;

Y is, independently for each occurrence, CO, CH_2, CS, or a bond;

R^1 is  ,  ,  , or $N(R^{24}R^{25})$;

R^2, R^{11}, and R^{12} each is, independently for each occurrence, H or an optionally substituted moiety selected from the group consisting of (C_{1-6})alkyl and

aryl, wherein said optionally substituted moiety is optionally substituted with one or more of R^8 or R^{30};

R^3 is, independently for each occurrence, H or an optionally substituted moiety selected from the group consisting of (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{2-6})alkynyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl(C_{1-6})alkyl, (C_{5-7})cycloalkenyl, (C_{5-7})cycloalkenyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, heterocyclyl, and heterocyclyl(C_{1-6})alkyl, wherein said optionally substituted moiety is optionally substituted with one or more R^{30};

R^4 and R^5 each is, independently for each occurrence, H or an optionally substituted moiety selected from the group consisting of (C_{1-6})alkyl, (C_{3-6})cycloalkyl, aryl, and heterocyclyl, wherein said optionally substituted moiety is optionally substituted with one or more R^{30}, wherein each said substituent is independently selected, or R^4 and R^5 can be taken together with the carbons to which they are attached to form aryl;

R^6 is, independently for each occurrence, H or an optionally substituted moiety selected from the group consisting of (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl (C_{1-6})alkyl, (C_{5-7})cycloalkenyl, (C_{5-7})cycloalkenyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, heterocyclyl, and heterocyclyl (C_{1-6})alkyl, wherein said optionally substituted moiety is optionally substituted with one or more substituents each independently selected from the group consisting of OH, (C_{1-6})alkyl, (C_{1-6})alkoxy, $-N(R^8R^9)$, -COOH, $-CON(R^8R^9)$, and halo,

where R^8 and R^9 each is, independently for each occurrence, H, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{2-6})alkynyl, aryl, or aryl(C_{1-6})alkyl;

R^7 is, independently for each occurrence, H, =O, =S, or an optionally substituted moiety selected from the group consisting of (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{3-6})cycloalkyl,

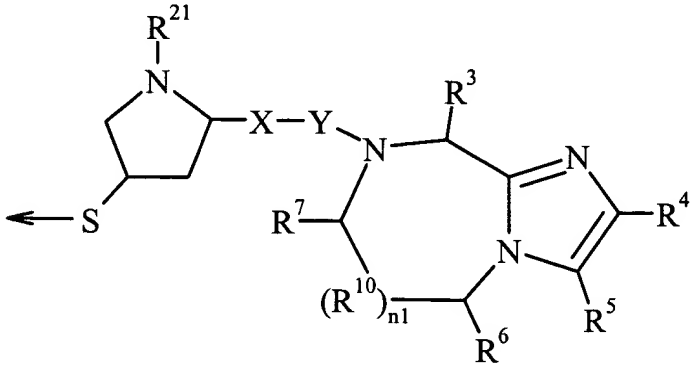
(C_{3-6})cycloalkyl(C_{1-6})alkyl, (C_{5-7})cycloalkenyl, (C_{5-7})cycloalkenyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, heterocyclyl, and heterocyclyl(C_{1-6})alkyl, wherein said optionally substituted moiety is optionally substituted with one or more substituents each independently selected from the group consisting of OH, (C_{1-6})alkyl, (C_{1-6})alkoxy, $-N(R^8R^9)$, -COOH, $-CON(R^8R^9)$, and halo;

R^{10} is C;

~~or when n1 = 0, R^6 and R^7 can be taken together with the carbon atoms to which they are attached to form aryl or cyclohexyl;~~

R^{21} is, independently for each occurrence, H or an optionally substituted moiety selected from the group consisting of (C_{1-6})alkyl and aryl(C_{1-6})alkyl, wherein said optionally substituted moiety is optionally substituted with one or more substituents each independently selected from the group consisting of R^8 and R^{30};

R^{22} is H, (C_{1-6})alkylthio, (C_{3-6})cycloalkylthio, R^8-CO-, or a substituent according to the formula



;

R^{24} and R^{25} each is, independently for each occurrence, H, (C_{1-6})alkyl, or aryl(C_{1-6})alkyl;

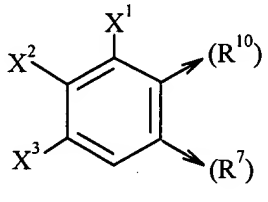
R^{30} is, independently for each occurrence, (C_{1-6})alkyl, $-O-R^8$, $-S(O)_{n6}R^8$, $-S(O)_{n7}N(R^8R^9)$, $-N(R^8R^9)$, -CN, $-NO_2$,

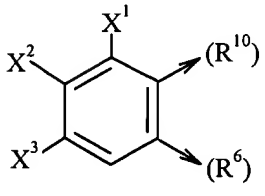
$-CO_2R^8$, $-CON(R^8R^9)$, $-NCO-R^8$, or halogen;

n6 and n7 each is, independently for each occurrence, 0, 1, or 2;

wherein said heterocyclyl is azepinyl, benzimidazolyl, benzisoxazolyl, benzofurazanyl, benzopyranyl, benzothiopyranyl, benzofuryl, benzothiazolyl, benzothienyl, benzoxazolyl, chromanyl, cinnolinyl, dihydrobenzofuryl, dihydrobenzothienyl, dihydrobenzothiopyranyl, dihydrobenzothio-pyranyl sulfone, furyl, imidazolidinyl, imidazolinyl, imidazolyl, indolinyl, indolyl, isochromanyl, isoindolinyl, isoquinolinyl, isothiazolidinyl, isothiazolyl, isothiazolidinyl, morpholinyl, naphthyridinyl, oxadiazolyl, 2-oxoazepinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, piperidyl, piperazinyl, pyridyl, pyridyl N-oxide, quinoxalinyl, tetrahydrofuryl, tetrahydroisoquinolinyl, tetrahydro-quinolinyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiazolyl, thiazolinyl, thienofuryl, thienothienyl, or thienyl; and wherein said aryl is phenyl or naphthyl;

provided that:

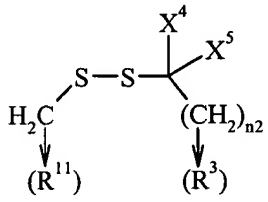
either R^6 is H or R^7 is =O, -H, or =S wherein when ~~n1 = 1, R^{10} is C and~~ R^6 is H, then R^{10} and R^7 are ~~can be~~ taken together to form 

; or when ~~n1 = 1, R^{10} is C, and~~ R^7 is =O, -H, or =S, then R^{10} and R^6 are ~~can be~~ taken together to form 

,

wherein X^1, X^2, and X^3 each is, independently, H, halogen, $-NO_2$, $-NCO-R^8$, $-CO_2R^8$, $-CN$, or $-CON(R^8R^9)$; and

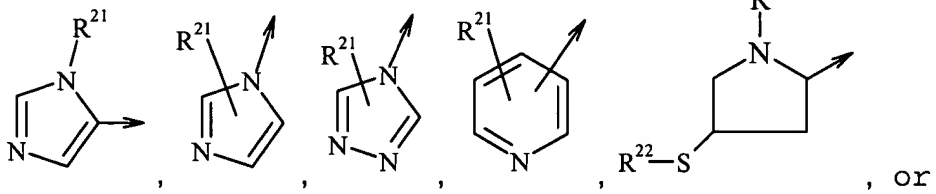
when R^1 is $N(R^{24}R^{25})$, then n3 is 1, n4 and n5 each is 0, Z is a bond, and R^3 and R^{11} can be taken together to form



wherein n2 is 1-6, and X^4 and X^5 each is, independently, H, (C_{1-6})alkyl, or aryl, or X^4 and X^5 can be taken together to form (C_{3-6})cycloalkyl;

or a pharmaceutically acceptable salt thereof.

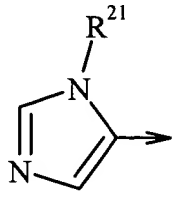
2 (original): A compound according to claim 1, wherein:

R^1 is  , or $N(R^{24}R^{25})$; and

X is $CH(R^{11})_{n3}(CH_2)_{n4}$ or Z, wherein Z is O, S, or $N(R^{12})$;

or a pharmaceutically acceptable salt thereof.

3 (withdrawn): A compound according to claim 2, wherein:

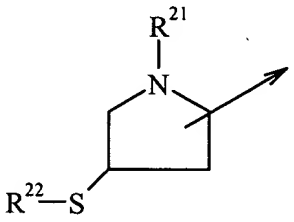
R^1 is  ;

X is $CH(R^{11})_{n3}(CH_2)_{n4}$; and

n1 is 0;

or a pharmaceutically acceptable salt thereof.

4 (withdrawn): A compound according to claim 2, wherein:

R^1 is  ;

n3, n4, and n5 each is 0;

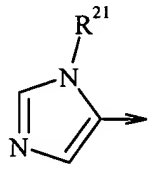
Z is a bond;

Y is, independently for each occurrence, CO or CS; and

n1 is 0;

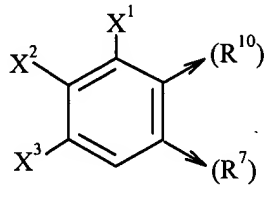
or a pharmaceutically acceptable salt thereof.

5 (original): A compound according to claim 2, wherein:

R^1 is  ;

R^6 is H;

n1 is 1;

R^7 and R^{10} are taken together to form  ;

n3 is 1 and R^{11} is H;

Z is O or a bond;

n5 is 0; and

Y is CO, CH_2, or a bond;

or a pharmaceutically acceptable salt thereof.

6 (withdrawn): A compound according to claim 2, wherein:

R^1 is $N(R^{24}R^{25})$;

n1 is 0;

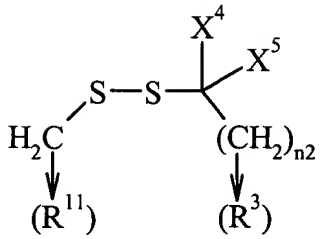
n3 is 1;

n4 is 0;

n5 is 0;

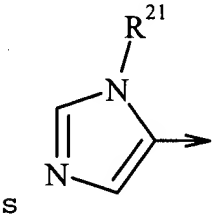
Y is CO or CS;

Z is a bond; and

R^3 and R^{11} are taken together to form 

, or a pharmaceutically acceptable salt thereof.

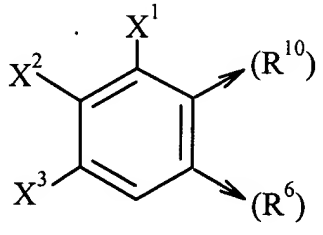
7 (original): A compound according to claim 2, wherein:

R^1 is 

;

R^7 is H or =O;

n1 is 1;

R^6 and R^{10} are taken together to form 

;

n3 is 1 and R^{11} is H;

n5 is 0;

Y is CO or CH_2; and

Z is O or a bond;
or a pharmaceutically acceptable salt thereof.

8 (withdrawn): A compound according to claim 3, wherein said compound is

8-butyl-7-(3-(imidazol-5-yl)-1-oxopropyl)-2-(2-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

8-butyl-2-(2-hydroxyphenyl)-7-(imidazol-4-yl-propyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

8-butyl-7-(4-imidazolylpropyl)-2-(2-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

7-(2-(imidazol-4-yl)-1-oxo-ethyl)-2-(2-methoxyphenyl)-8-(1-methylpropyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

2-(2-methoxyphenyl)-8-(1-methylpropyl)-7-(1-oxo-2-(1-(phenylmethyl)-imidazol-5-yl)ethyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

2-(2-methoxyphenyl)-8-(1-methylpropyl)-7-(2-(1-phenylmethyl)-imidazol-5-yl)ethyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

7-(2-(1-(4-cyanophenylmethyl)-imidazol-5-yl)-1-oxo-ethyl)-2-(2-methoxyphenyl)-8-(1-methylpropyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

7-((1H-imidazol-4-yl)methyl)-2-(2-methoxyphenyl)-8-(1-methylpropyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

7-((4-imidazolyl)carbonyl)-2-(2-methoxyphenyl)-8-(1-methylpropyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

7-(1-(4-cyanophenylmethyl)-imidazol-5-yl)methyl-2-(2-methoxyphenyl)-8-(1-methylpropyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

7-(2-(4-cyanophenylmethyl)-imidazol-5-yl)-1-oxo-ethyl)-2-(2-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine;

5-butyl-7-(2-(4-cyanophenylmethylimidazol-5-yl)-1-oxo-ethyl)-2-phenyl-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

6-butyl-7-(2-(4-cyanophenylmethylimidazol-5-yl)-1-oxo-ethyl)-2-(2-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine;

6-butyl-7-(2-(4-cyanophenylmethylimidazol-5-yl)-1-oxo-ethyl)-2-phenyl-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine;

5-butyl-7-(2-(1-(4-cyanophenylmethyl)-imidazole-5-yl)-1-oxo-ethyl)-2-(2-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

7-(2-(1-(4-cyanophenylmethyl)-imidazole-5-yl)-1-oxo-ethyl)-8-(cyclohexylmethyl)-2-(2-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

5-butyl-7-(2-(1H-imidazole-5-yl)-1-oxo-ethyl)-2-(2-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine;

7-(2-(4-cyanophenylmethyl)-imidazol-5-yl)-1-oxo-ethyl)-2-(2-(phenylmethoxy)-phenyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine; or

2-(2-butoxyphenyl)-7-(2-(4-cyanophenylmethyl)-imidazol-5-yl)-1-oxo-ethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine; or a pharmaceutically acceptable salt thereof.

9 (currently amended): A compound according to claim 5, wherein said compound is

1,2-dihydro-1-((1H-imidazol-4-yl)methyl)-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine;

1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine ;

9-bromo-1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine;

9-chloro-1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine;

10-bBromo-1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine; or

1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-8-fluoro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine; ~~or~~

or a pharmaceutically acceptable salt thereof.

10 (currently amended): A compound according to claim 9, wherein said compound is

1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine;

9-bromo-1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine;

9-cChloro-1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine;

10-bBromo-1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine; or

1-(2-(1-(4-cyanophenylmethyl)imidazol-4-yl)-1-oxoethyl)-1,2-dihydro-8-fluoro-4-(2-methoxyphenyl)-imidazo[1,2-c][1,4]benzodiazepine;

or a pharmaceutically acceptable salt thereof.

11 (withdrawn): A compound according to claim 6, wherein said compound is

7-(2-amino-1-oxo-3-thiopropyl)-8-(mercaptoethyl)-2-(2-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine disulfide;

or a pharmaceutically acceptable salt thereof.

12 (original): A compound according to claim 7, wherein said compound is

5-(2-(1-(4-cyanophenylmethyl)-imidazol-5-yl)-1-oxo-ethyl)-5,6-dihydro-2-phenyl-1H-imidazo[1,2-a][1,4]benzodiazepine;

or a pharmaceutically acceptable salt thereof.

13 (original): A compound according to claim 2 wherein said compound is

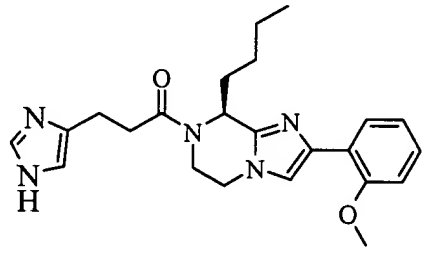
1,2-dihydro-1-(2-(imidazol-1-yl)-1-oxoethyl)-4-(2-methoxyphenyl) imidazo[1,2a][1,4]benzodiazepine;

1,2-dihydro-4-(2-methoxyphenyl)-1-(2-(pyridin-3-yl)-1-oxoethyl) imidazo[1,2a][1,4]benzodiazepine; or

1,2-dihydro-4-(2-methoxyphenyl)-1-(2-(pyridin-4-yl)-1-oxoethyl) imidazo[1,2a][1,4]benzodiazepine;

or a pharmaceutically acceptable salt thereof.

14 (original): A compound according to claim 2, wherein said compound is



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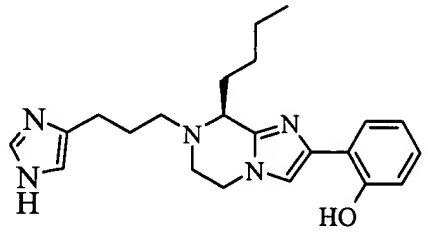

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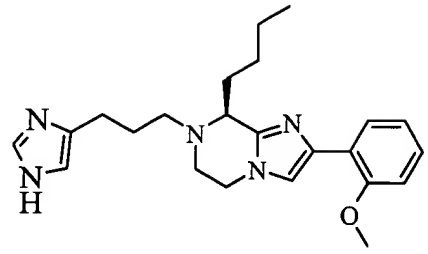
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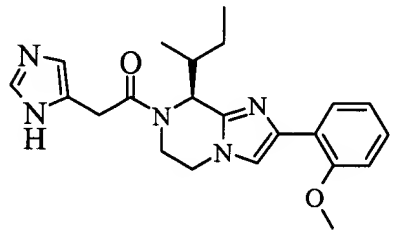
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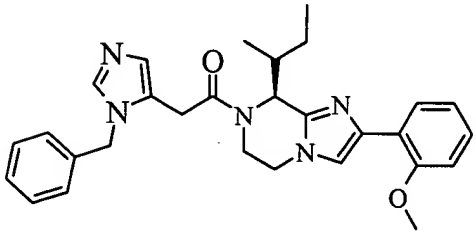
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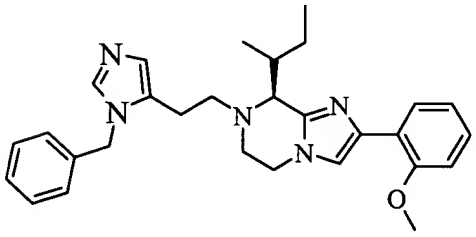
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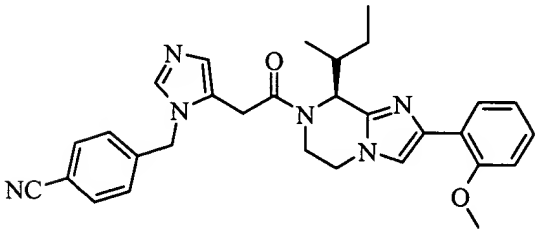
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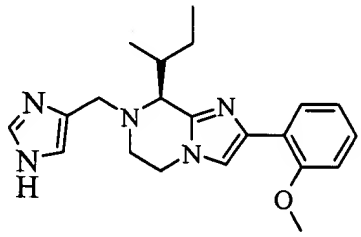
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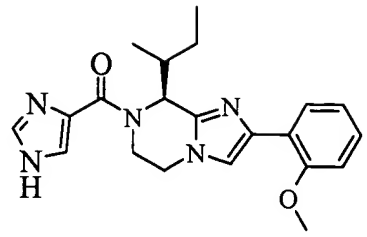
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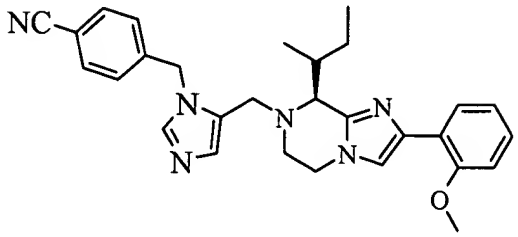
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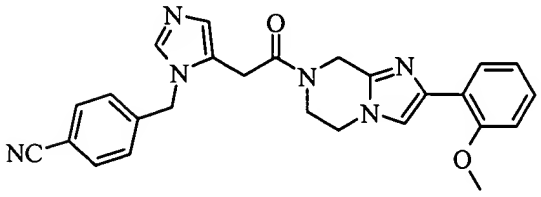
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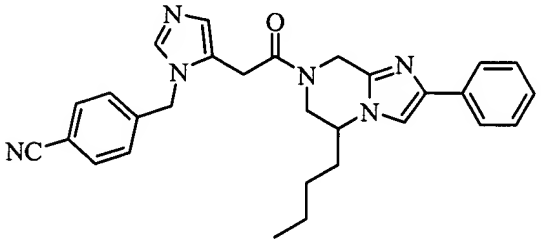
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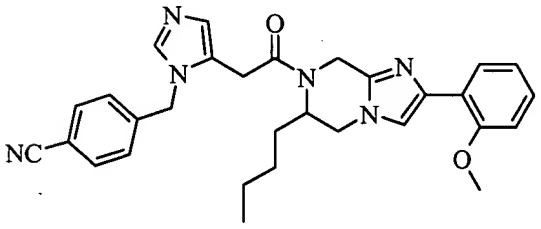
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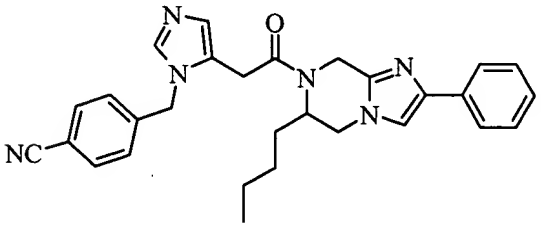
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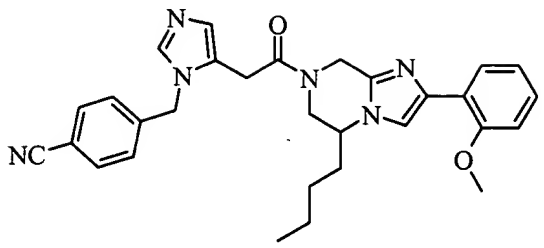
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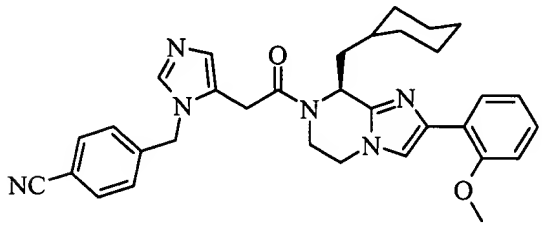
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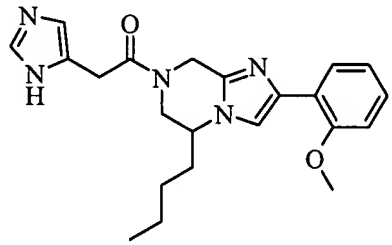
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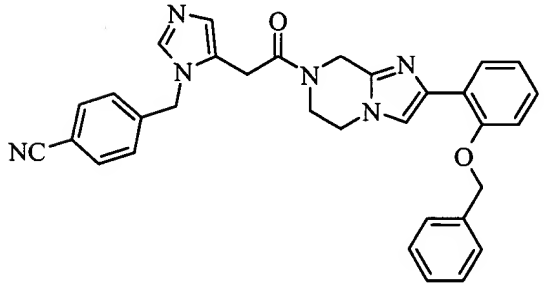
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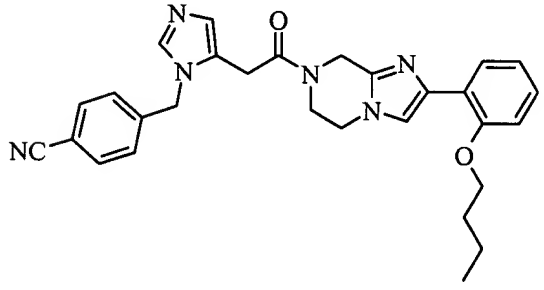
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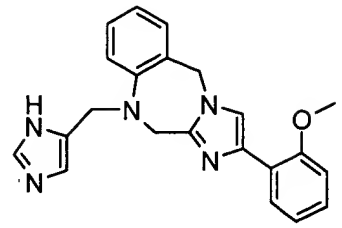
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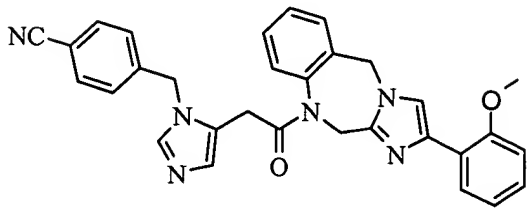
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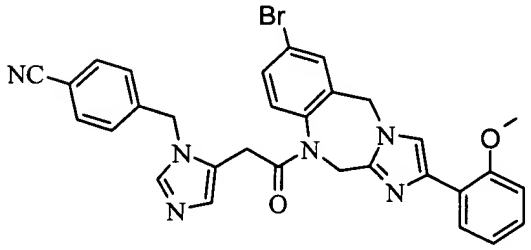
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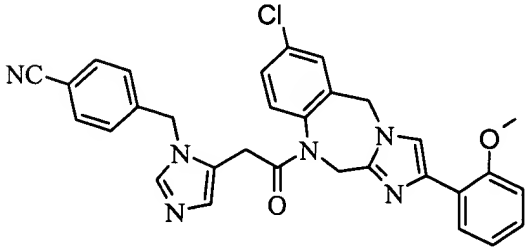
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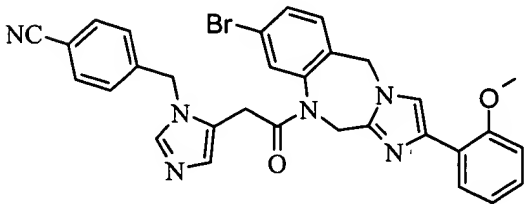
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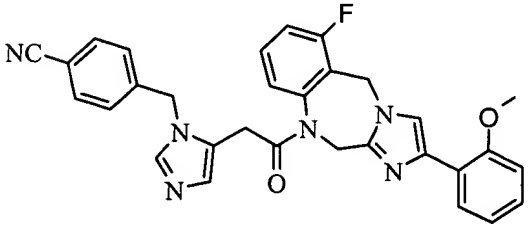
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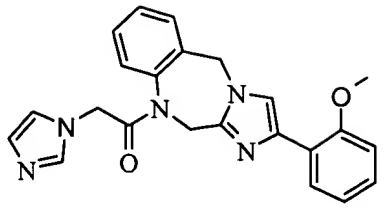
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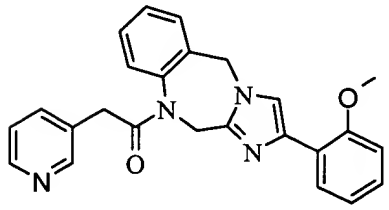
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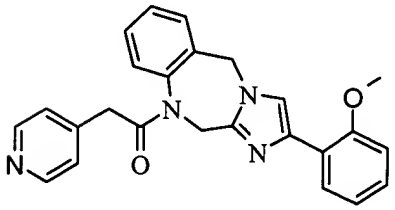
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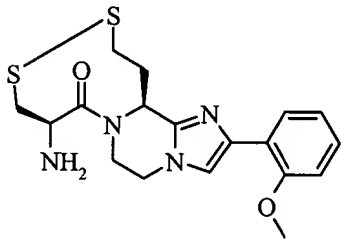
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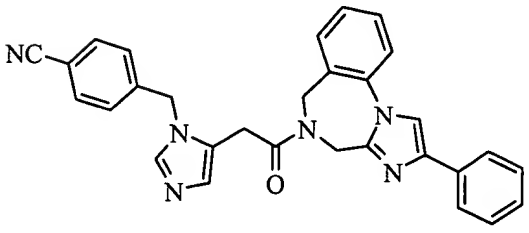
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or a pharmaceutically acceptable salt thereof.

15 (currently amended): A pharmaceutical composition for use in treating a disease selected from the group consisting of breast cancer, colon cancer, pancreas cancer, prostate cancer, lung cancer, ovarian cancer,

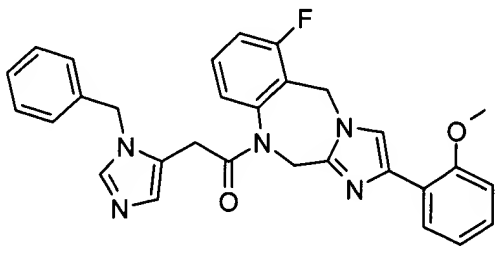
epidermal cancer and hematopoietic cancer, comprising an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

16 (currently amended): A method of treating a disease in a subject in need thereof, said method comprising administering to said subject a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein said disease is selected from the group consisting of ~~fibrosis, benign prostatic hyperplasia, atherosclerosis, restenosis,~~ breast cancer, colon cancer, pancreas cancer, prostate cancer, lung cancer, ovarian cancer, epidermal cancer~~,~~ and hematopoietic cancer~~,~~ ~~and hepatitis delta virus infection~~.

17 (canceled)

18 (canceled)

19 (original): A compound according to claim 2, wherein said compound is



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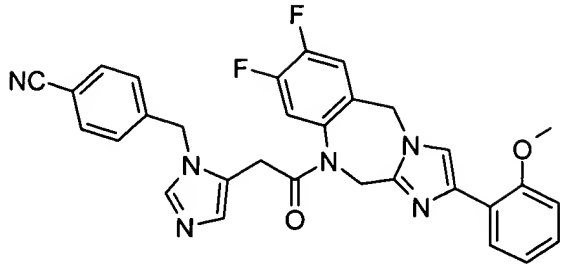
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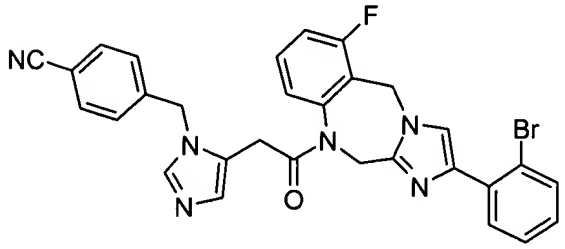
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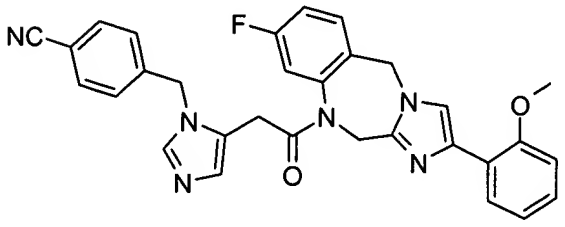
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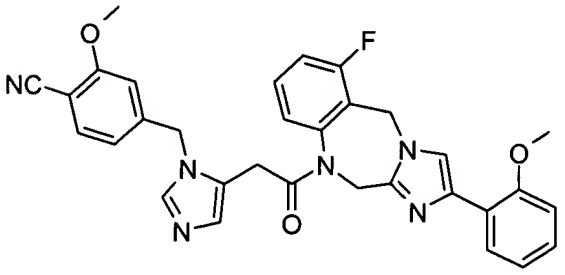
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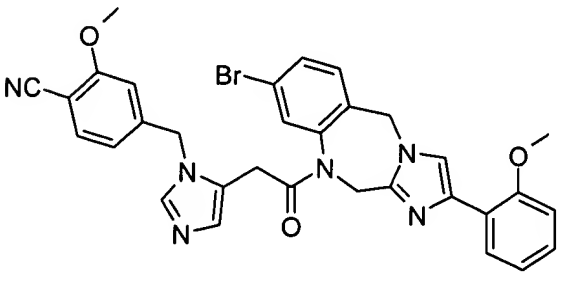
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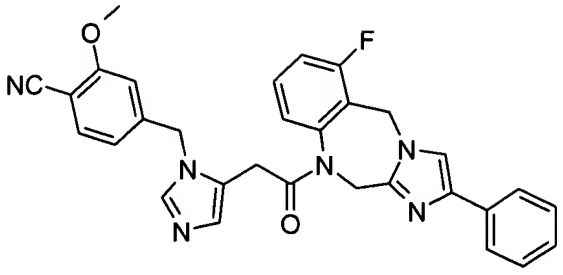

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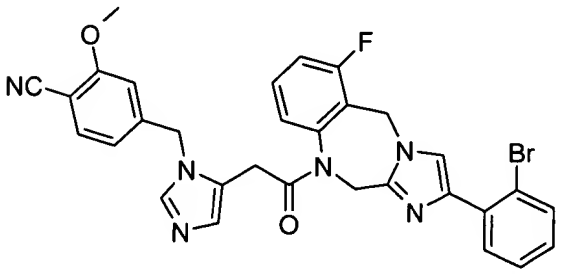

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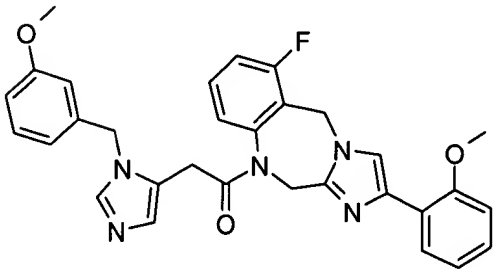

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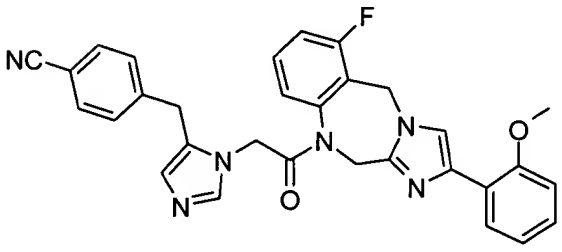

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or a pharmaceutically acceptable salt thereof.

--20 (new): A pharmaceutical composition for use in treating a disease selected from the group consisting of fibrosis, benign prostatic hyperplasia, atherosclerosis, restenosis and hepatitis delta virus infection comprising an

effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

21 (new): A method of treating a disease in a subject in need thereof, said method comprising administering to said subject a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein said disease is selected from the group consisting of fibrosis, benign prostatic hyperplasia, atherosclerosis, restenosis and hepatitis delta virus infection.--